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Objective: To establish physiological base line data, and to develop physiological procedures and instrumentation necessary for the automatic measurement of hemodynamic and metabolic parameters during prolonged periods of weightlessness.

Status: A total of 42 monkeys comprised the colony at the conclusion of this report period. The condition of the colony continued to be satisfactory and pathological organisms were not found to be a direct causative factor in the demise of any colony member. The major portion of the physiological data reported herein was obtained from pig-tailed monkeys; however, some experimental surgery has been carried out on rhesus monkeys.

Reproduction and Growth. The outdoor breeding colony consists of one male and four female pig-tailed monkeys. The first generation of offspring (3 males and 1 female) have been removed from this area and placed in individual cages for closer observation and frequent handling. Preliminary observations of these young animals, aged 6 months to 18 months, tend to indicate that they will be more suitable as future

experimental physiological subjects than animals obtained from the wild state; in particular, they are healthier and are easier to handle, as well as being of precisely known ages.

Female pig-tailed monkey #31, Dorcas, gave birth to an apparently normal healthy female on 23 February 1965, her second offspring in the colony. Unfortunately this infant succumbed to unknown causes on 30 March 1965. The infant did not appear to be suffering from any nutritional deficiency. Body weight was within the best estimation of the norm for this particular stage of growth. Radiological examination failed to reveal a cause for death. Interestingly, this was the second parturition within a year for #31, Dorcas. Previously she had given birth to male #51, Cornelius, on 3 March 1964.

These animals of known birth date are being weighed twice weekly. Gross anthropometric measurements and radiological examinations are made once each month.

Behavioral Studies. An initial attempt has been made to adapt techniques and methods used currently in behavioral studies of sub-human primates to our pig-tailed monkeys restrained in contour couches and confined in individual isolation boxes.

A miniature test apparatus, 6 inches long by 5 inches wide, containing small food bins with sliding covers, has been devised to fit into the space occupied by the monkeys' daily food ration. To start with, small food pellets approximately 250 mg in weight were placed in the open bins, and the monkeys quickly learned to pick them up. Next, pellets were placed in all three bins and the sliding covers closed. In their random play with the top of the tray the monkeys again quickly discovered that food pellets were to be found under the sliding covers.

At this point the animals were ready to start learning trials. These consisted of placing a food pellet in only one bin, always under the same pattern but random in position, and counting the number of times the monkey chose the correct bin in a succession of 20 presentations.

After the preliminary training, two monkeys, #58, Pindarus and #82, Bushy, were tested daily for a period of three weeks. Approximately 60-90 trials were run each day. At the initiation of the tests both monkeys had been in contour couch restraint for a period in excess of two months. The first problem tried with the miniature apparatus was a black-white discrimination using equilateral ($5/8$ " to a side) cardboard triangles attached to the sliding covers of the food bins. Stimuli were varied from right to left position such that position could not influence his choice. In addition to simple discrimination tests, reversal trials were also carried out. The results of the various tests are shown in Tables 1 and 2.

It has been reported in the literature that two-dimensional representations are more difficult for monkeys to learn to discriminate than are three-dimensional objects of the same shape. Therefore, small three-dimensional stimulus objects not exceeding one inch in their greatest dimension, consisting specifically of a star, two circles of different diameters, a diamond, and a rectangle, were used for trials on a third monkey #68, Alexas. The results are shown in Table 3. This monkey was a very fast learner for a naive subject as compared to the data from extant literature on monkey experiments. Usually when discriminations and their reversals are learned as fast as the "circle-star" was by #68, Alexas, they are reported for highly trained monkeys who have previously solved hundreds of discrimination problems.

Results to date on these three monkeys tend to indicate that the miniature test tray is a valid method of testing monkeys in the isolation boxes on various types of discrimination, discrimination reversal, oddity, matching and probability problems.

Plasma Clearance of Indocyanine Green. The clearance time of indocyanine green was measured on three male pig-tailed monkeys. Preliminary trials were conducted to determine optimum sampling intervals and the minimum amount of dye which may be injected to produce reliable results. Vascular catheters had previously been implanted, and the animals had been in couch restraint for periods of time varying from one week to two months. Prior to dye injection a blood sample was removed from the arterial catheter for the preparation of a blank and standard. The dye was introduced by way of the venous catheter at a level of 0.5 mg/kg of body weight. Blood samples were withdrawn from the arterial catheter at 1.0, 1.5, 2.0 and 3.0 minutes after injection of the dye. The blood was centrifuged at 2200 rpm for 10 minutes and the plasma layer removed. The optical density of each plasma sample was read on a Beckman DU spectrophotometer at a wave-length of 805 μ , the absorption maximum for indocyanine green. The concentration of the dye in mg/100 ml of plasma was calculated and plotted against time on 2-cycle semilogarithmic graph paper. A straight line was fitted to the exponential portion of the curve, and its slope represented k in the equation: $\ln(C_o/C_t) = kt$. The clearance half-time of the dye is given by the relationship $t_{1/2} = \frac{\ln 2}{k}$. The value, C_o , could also be determined by extrapolation back to zero time and plasma volume could be computed from the formula:

$$\text{plasma volume (ml)} = \text{dye injected (mg)} / C_o \text{ (mg/ml)}$$

Results are shown in Table 4. For comparison, estimated plasma volumes calculated as 5% of body weight are included. Owing to the very rapid clearance of indocyanine green from the plasma of the pig-tailed monkey, use of this dye for the determination of plasma volume may yield inaccurate values. Comparison of the indocyanine method with the more conventional use of Evans Blue (T-1824) for plasma volume measurements are in progress.

Biotelemetry. A calibrated temperature sensor and transmitter, furnished by Winget and Fryer of the NASA Ames Research Center, was surgically implanted in pig-tailed monkey #3, Tybalt. The sensor was positioned to record body temperatures which could be compared directly to rectal temperatures obtained by thermistor probe from the lower portion of the colon. Following surgery, the animal was returned to a cage measuring 28 inches high, 28 inches wide and 34 inches deep. The cage was equipped on 3 sides with a wire antenna. Signals from the transmitter were picked up by a receiver, demodulated and recorded continuously. A summary of one series of telemetered temperature data from #3, Tybalt is shown in Table 5. A definite diurnal variation is demonstrated. Also, definite changes in pattern may be noted for Saturday, 13 February and Sunday, 14 February. While a constant 12 hours on, 12 hours off light cycle was maintained throughout the week, levels of activity in the surrounding laboratory area were diminished on the weekend from those occurring during the balance of the week.

Several body temperature telemetry devices have been manufactured in our laboratory. Numerous types of potting compounds for transmitter circuit components have been tested in vivo in monkeys for long term stability with varying results. While some of our units have performed well in controlled temperature saline baths, capacitance changes which

have occurred following surgical implantation have seriously limited the usefulness of the transmitted signal. It appears, however, that the Ames design is successful and will meet the long term requirements of this project.

Urine Collection. Flat Teflon rings of 4 cm outer diameter, 3 cm inner diameter and 2 mm thick with 4 screw-threaded raised areas, were inserted subcutaneously surrounding the base of the penis in two male rhesus monkeys. One week later the threaded portions were exposed and a Lapidus urinary ileostomy bag was attached with stainless steel screws and a matching outer Teflon ring. The monkeys were then jacketed and restrained in a contour couch. A tube was connected to the distal end of the bag and led to a collection flask. Clear, non-fecal exposed urine was collected for 29 days from #99, Grenvil and for 12 days from #100, Douphol. The trials were terminated by the appearance of ischemic areas in the skin near the bag attachment. The collection bag was removed and the animals returned to cages with the inner Teflon ring intact. This procedure may allow quantitative collection of urine for periods up to one month without the need for major surgery, but suffers from the limitation that collection is dependent upon bladder contraction and hence is sporadic. A pattern of micturition was determined for the rhesus monkey #99, Grenvil, by attaching a urine collection device which fractionated eight 3-hour samples during 24 hours. The results are shown in Table 6. The largest voiding occurred during the morning at approximately 0700 hours. No voiding occurred during the night.

Attention has also been given to improvement of biochemical methods of urine analysis. Conventional methods for many urine constituents require a sample size that precludes analysis in the relatively small

volumes of urine produced by the monkey. A systematic modification and scaling down of standard methods for urine analysis is being carried out. Thus far, microchemical procedures have been developed which permit the quantitative determination of 12 constituents in a total urine volume of approximately 0.5 ml. These constituents are: ammonia, urea, creatinine, creatine, phosphate, uric acid, glucose, chloride, calcium, magnesium, sulfate and titratable acidity.

Preliminary trials have been conducted with a miniature flow-through reflecting refractometer. There appears to be a high correlation between signal output and total solute concentration when urine is passed through the device. The apparatus contains no moving parts, and may find good application for in-flight, on-line urine analysis. It is also planned to use this principle for on-line plasma protein determinations.

Hemodynamics. Three pig-tailed monkeys #58, Pindarus, #62, Bushy and #68, Alexas were continuously restrained in contour couches and isolation boxes for periods of at least ninety days. Hemodynamic measurements were made during the same time (afternoon) on Wednesdays and Fridays of each week. Care was taken to keep the environment quiet during the measurement periods. Direct blood pressure measurements were recorded for 2 to 4 hours during each trial. Three cardiac output determinations using the dye dilution method were made at 15 minute intervals during the course of each trial. Tables 7, 8 and 9 contain the hemodynamic data resulting from the ninety day experiments. No exaggerated hemodynamic changes appeared to take place during the course of the experiment. Cardiac output and cardiac work tended to rise shortly after the start of the confinement, then gradually decreased as the confinement progressed. At the end of the 90 day confinement period the monkeys

exhibited leg weakness upon being released into their cages, and approximately a month was required for them to regain full locomotor function.

The effect of blood withdrawal was evaluated on #62, Bushy and the results are shown in Table 10. In a series of trials, varying amounts of blood from 13.5 to 30 ml were withdrawn by the same procedure used for cardiac output determinations. This monkey had electrocardiographic chest leads attached, and heart rate could be recorded during all phases of the blood withdrawal and injection. Blood pressures were measured immediately before blood withdrawal, for one minute after withdrawal, and immediately following return of blood to the experimental subject. Even the largest withdrawal, 30 ml, did not measurably affect either the heart rate or the blood pressure of this 9.0 kg monkey. Inasmuch as only about 15 ml of blood are withdrawn and returned during the usual cardiac output determination, it seems clear that no significant alteration in hemodynamics occurs as a result of the cardiac output measurement procedure.

A twenty-four hour cardiac output trial was conducted on the pig-tailed monkey #56, Titinius. A chronically implanted pulmonary arterial catheter was used for dye injection, while blood was withdrawn from a left atrial catheter. Cardiac output determinations were made every hour during the 24-hour trial. As shown in Table 11 a slight diurnal variation was noted, with higher cardiac outputs occurring between 1700 and 2400 hours. The measurements on #56, Titinius were made during the 182nd and 183rd day of couch confinement.

Hemodynamic measurements on #68, Alexas were similarly made for 24 hours during his second and third days of couch confinement. Heart rate and blood pressures showed a diurnal variation with a decrease during the early morning hours. The hourly results of this trial are shown in Table 12.

In order to evaluate the method of computation of cardiac output used in this laboratory, two preliminary approaches, estimated to produce changes in hemodynamic activity, have been tried. In one case the drug, isoproterenol (Isuprel), which is known to increase cardiac output, was used. In the second case hypothermia, which is known to decrease cardiac output, was induced. Chronically vascular catheterized pig-tailed monkeys were the experimental animals in both instances.

The results of the drug action on #68, Alexas are shown in Table 13. Isoproterenol was injected by way of the arterial catheter rather than on the venous side, in order that an accurate amount of indocyanine green dye could be introduced into the vena cava for a cardiac output determination as soon as possible after the drug took effect. At injection levels of 0.02 and 0.032 mg, the drug immediately reduced systemic resistance and increased heart rate and cardiac output, while stroke volume and aortic blood pressures remained relatively unchanged.

A hypothermia trial (Table 14) was performed on the male pig-tailed monkey #55, Verges. During the course of this trial, rectal temperature was reduced from 35.2°C following initial anesthesia with an intravenous injection of Brevital, to a level of 25.6°C with a cooling blanket. Aortic pressures remained unchanged while cardiac output was reduced by a factor of slightly more than one-half.

Modifications are being made in the prototype hemodynamic measuring system originally designed and built in cooperation with the Technical Services Directorate of the Headquarters, Pacific Missile Range at Point Mugu, California. Troublesome air leaks in the original blood withdrawal syringe mechanism have been eliminated. Changes on the face of the plunger, allowing a more effective cleansing action, have been

made. Various blood pressure transducers have been investigated, but none has been found to date which is satisfactory. Design of a suitable pressure transducer is in progress.

Total Body Water: Total body water was measured for pig-tailed monkey #58, Pindarus. Including this animal, total body water content has now been determined by the tritiated water method on eight pig-tailed monkeys. All of the results are summarized in Table 15. Per cent body fat was computed from the relationship:

$$\% \text{ fat} = 100 - \% \text{ water}/0.732$$

Clearance half-time of the tritiated water from the body was also determined, and is shown in Table 15.

Table 1. Discrimination between Black and White Triangles
as Learned by Pig-Tailed Monkey #58, Pindarus.

Block of 20 Trials	A Original Learning: White Triangle Rewarded			B First Reversal: Black Triangle Rewarded			C Second Reversal: White Triangle Rewarded		
	No.correct per 20 trials			No.correct per 20 trials			No.correct per 20 trials		
	0-6	(7-13)	14-20	0-6	(7-13)	14-20	0-6	(7-13)	14-20
1-20	X*			X			X		
21-40	X			X			X		
41-60			X	X			X		
61-80			X	X			X		
81-100			X	X			X		
101-120			X	X				X	
121-140			X		X			X	
141-160	X			X				X	
161-180			X	X				X	
181-200	X			X				X	
201-220			X	X				X	
221-240			X	X				X	
241-260			X	X				X	
261-280			X	X				X	
281-300				X					X
301-320				X				X	
321-340				X				X	
341-360						X		X	
361-380				X					X
381-400				X					X
401-420						X			X
421-440						X			X
441-460				X					X
461-480						X			X
481-500						X		X	
501-520						X			X

* X's indicate that the actual number of correct choices in the total of 20 trials fell into the range shown. The range (7-13) is taken to represent chance performance; i.e., the monkey could be choosing right or left consistently, or choosing white or black randomly.

Table 2. Discrimination between Black and White Triangles
as Learned by Pig-Tailed Monkey #62, Bushy

Block of 20 Trials	A Original Learning: White Triangle Rewarded No.correct per 20 trials			B First Reversal: Black Triangle Rewarded No.correct per 20 trials			C Second Reversal: White Triangle Rewarded No.correct per 20 trials		
	0-6	(7-13)	14-20	0-6	(7-13)	14-20	0-6	(7-13)	14-20
	1-20		X*		X			X	
21-40		X		X			X		
41-60		X			X		X		
61-80		X			X			X	
81-100		X			X			X	
101-120		X			X			X	
121-140		X			X			X	
141-160	X				X		X		
161-180			X		X			X	
181-200			X		X			X	
201-220			X		X			X	
221-240		X			X				X
241-260			X		X			X	
261-280			X		X			X	
281-300			X		X			X	
301-320					X				X
321-340					X				X
341-360					X				X
361-380					X				X
381-400						X		X	
401-420						X		X	
421-440					X				X
441-460						X			X
461-480					X			X	
481-500						X		X	
501-520						X		X	
521-540						X			X
541-560						X			X
561-580						X	X		
581-600						X		X	

* X's indicate that the actual number of correct choices in the total of 20 trials fell into the range shown. The range (7-13) is taken to represent chance performance; i.e., the monkey could be choosing right or left consistently, or choosing white or black randomly.

Table 4. Blood Plasma Clearance Half-Time of Indocyanine Green in Pig-Tailed Monkeys, and Associated Plasma Volume Estimates.

Animal No. & Name	Plasma Clearance Half-Time $t_{1/2}$ (min)	Body Weight (kg)	Plasma Volume from C_0 (ml)	Plasma Volume Computed as 5% of Body Weight (ml)
#70, Seleucus	1.77	7.91	364	395
#68, Alexas	1.17	5.35	309	267
#58, Pindarus	2.20	8.00	362	400

Table 5. Body Temperature ($^{\circ}\text{C}$) Telemetered from an Implanted Transmitter in the Abdominal Cavity of Pig-Tailed Monkey #3, Tybalt, Free in a Cage during February 1965.

Time of Day	Date	8 Mon	9 Tues	10 Wed	11 Thurs	12 Fri	13 Sat	14 Sun	15 Mon	16 Tues	17 Wed	18 Thurs	19 Fri
0100			37.6	37.5	-	36.6	36.8	36.8	37.0	-	-	36.9	36.9
0200			37.6	37.5	-	36.5	36.8	36.8	37.0	-	-	36.9	36.9
0300			37.5	37.5	-	36.7	36.8	37.0	37.0	-	-	37.0	36.8
0400			37.6	37.5	-	36.7	36.7	37.2	37.3	-	-	37.0	36.8
0500			37.6	37.7	-	36.7	36.8	37.2	37.3	-	-	37.0	36.8
0600			37.3	37.6	-	36.9	36.8	37.2	37.3	-	-	36.9	36.8
0700			37.4	37.6	37.2	36.8	36.8	37.2	37.3	38.4	37.8	38.0	37.6
0800			38.1	38.1	37.8	38.0	36.8	37.3	38.5	38.5	38.4	38.5	End of
0900			38.7	38.6	38.4	38.4	37.0	37.4	38.7	38.5	38.4	38.2	trans-
1000			38.7	38.8	38.3	38.3	37.1	37.2	38.7	38.7	38.3	38.5	mission
1100			38.7	-	38.8	38.5	37.6	37.5	38.5	38.6	38.2	38.3	
1200			38.6	-	38.5	38.2	37.7	37.8	38.3	38.2	38.0	38.2	
1300			38.7	-	38.6	38.5	38.1	38.5	38.5	38.3	38.3	38.5	
1400			38.8	-	38.7	38.4	37.5	38.1	38.6	38.7	38.5	38.6	
1500			38.7	38.9	38.7	38.6	37.5	38.8	38.7	38.7	38.5	38.5	
1600	Start		38.9	38.8	38.6	38.5	37.6	38.9	38.5	38.5	38.7	38.6	
1700		38.8	38.9	38.5	38.8	38.0	37.1	37.7	37.9	38.2	38.1	38.1	
1800		38.5	38.4	37.8	38.0	-	36.9	36.9	37.8	37.8	37.8	37.7	
1900		38.2	38.1	37.6	37.6	-	36.8	37.5	37.7	37.4	37.5	37.7	
2000		38.1	37.8	37.4	37.2	-	36.8	37.0	37.1	37.3	37.2	37.2	
2100		37.9	37.7	-	37.0	-	36.8	37.0	37.0	37.1	37.1	37.0	
2200		37.8	37.6	-	36.8	-	36.7	36.9	-	37.1	37.0	36.8	
2300		37.8	37.6	-	36.6	-	36.8	36.8	-	37.0	36.8	36.8	
2400		37.7	37.6	-	36.6	-	36.8	37.0	-	37.0	36.9	36.9	

Table 6. Daily Urine Excretion Pattern and Daily Totals of Water Consumption, Urine Production, Food Consumption and Feces Production in Male Rhesus Monkey #99, Grenvil, Body Weight 5.85 kg.

Time Periods	30 June 65 Vol. Spec. (ml) Grav.	1 July 65 Vol. Spec. (ml) Grav.	2 July 65 Vol. Spec. (ml) Grav.	3 July 65 Vol. Spec. (ml) Grav.	4 July 65 Vol. Spec. (ml) Grav.
(1) 0001-0300		0	0	0	NR*
(2) 0301-0600		0	0	0	NR
(3) 0601-0900		146	184	154	NR
(4) 0901-1200	Start	40	29	NR	21
(5) 1201-1500	36 } 1.011	75	31 } 1.015	NR	2 } 1.016
(6) 1501-1800	36	58	0	NR	25
(7) 1801-2100	0	0	0	NR	0
(8) 2101-2400	0	0	0	NR	0
24-Hour Totals		480	NR	350	370
Water Consumption (ml)		319	244	NR	NR
Urine Production (ml)		150	150	150	150
Food† Consumption (g)		74	NR	NR	NR
Feces Production (g)					
(1) 0001-0300	5 July 65	6 July 65	7 July 65	8 July 65	9 July 65
(2) 0301-0600	0	0	0	0	0
(3) 0601-0900	184	281	158	183	192
(4) 0901-1200	25 } 1.016	27 } 1.012	17 } 1.016	19	1.009
(5) 1201-1500	58 } 1.012	14 } 1.011	19 } 1.011	67	End of trial
(6) 1501-1800	29 } 1.012	0	28 } 1.011	17	
(7) 1801-2100	0	0	0	0	
(8) 2101-2400	0	0	0	0	
24-Hour Totals	450	350	380	420	
Water Consumption (ml)	296	322	222	286	
Urine Production (ml)	150	150	NR	150	
Food† Consumption (g)	NR	68	32	65	
Feces Production (g)					

* NR = not recorded

† Purina Monkey Chow

Table 7A. Hemodynamic Data from Pig-Tailed Monkey #62, Bushy, during Continuous Restraint.
Aortic Blood Pressures and Heart Rate.

Date	Couch Day	Aortic Pressures				Heart Rate	
		Systolic Mean Range (mm Hg)	Diastolic Mean Range (mm Hg)	Pulse Mean Range (mm Hg)	Mean Range (mm Hg)	Mean Range (beats/min)	
17 Feb 65	2	146 142-152	89 84-96	57 55-59	119 117-125	177 174-180	
19 Feb	4	154 151-158	87 85-88	67 63-71	123 120-125	163 160-168	
24 Feb	9	169 160-175	98 92-103	71 68-72	136 130-139	204 202-206	
26 Feb	11	166 162-170	95 92-98	71 69-74	129 127-132	201 196-208	
3 Mar	16	147 143-149	83 81-86	64 62-67	114 111-119	193 190-196	
10 Mar	23	149 147-150	85 84-87	64 63-65	116 115-118	186 184-188	
12 Mar	25	149 149-150	85 81-91	64 59-68	118 115-120	181 176-188	
17 Mar	30	150 150-150	89 88-90	61 60-62	115 110-117	175 172-180	
19 Mar	32	159 151-172	93 88-101	66 60-71	125 121-131	185 180-188	
24 Mar	37	151 176-180	87 84-89	64 60-67	118 117-119	179 176-180	
26 Mar	39	144 141-147	79 77-82	66 64-68	110 107-112	187 184-190	
31 Mar	44	141 135-150	82 77-86	59 53-64	109 107-112	160 152-164	
2 Apr	46	143 136-148	82 77-87	61 59-63	112 107-115	167 156-176	
7 Apr	51	138 132-143	76 75-77	63 57-68	105 101-108	174 168-178	
9 Apr	53	136 131-139	78 77-80	54 51-57	106 105-107	167 164-170	
14 Apr	58	147 145-150	87 85-88	60 58-61	117 117-117	184 180-188	
16 Apr	60	135 129-142	82 80-85	53 49-57	103 100-108	169 162-180	
21 Apr	65	158 156-161	93 90-97	65 64-66	125 125-125	187 184-188	
23 Apr	67	139 134-147	82 76-90	58 57-58	112 108-118	171 164-182	
28 Apr	72	137 130-144	77 75-79	58 55-61	110 105-115	184 180-188	
30 Apr	74	136 131-141	78 74-83	58 57-59	105 100-110	172 168-176	
5 May	79	146 141-154	88 81-95	58 46-66	115 110-120	197 192-202	
7 May	81	142 132-150	82 76-89	60 56-61	112 105-120	187 180-192	
12 May	86	144 130-150	80 75-86	58 55-64	108 102-120	183 178-192	
14 May	88	141 135-147	80 78-83	61 57-64	104 107-112	173 168-178	
19 May	93	146 142-148	86 85-87	60 57-62	115 112-117	171 170-172	

Table 7B. Hemodynamic Data from Pig-Tailed Monkey #62, Bushy, during Continuous Restraint. Cardiac Output, Stroke Volume, Mean Venous Pressure, Systemic Resistance and Cardiac Work.

Date	Couch Day	Cardiac Output		Stroke Volume		Mean Venous Pressure		Systemic Resistance		Cardiac Work	
		Mean (liters/min)	Range	Mean (ml)	Range	Mean (mm Hg)	Range	Mean (dyne sec/cm ⁵)	Range	Mean (watts)	Range
17 Feb 65	2	0.76	.74-.78	4.3	4.3-4.4	-2	-2 to -2	12,700	12,300-13,200	.202	.190-.216
19 Feb	4	0.92	.78-1.06	5.6	4.6-6.6	+1	+2 to 0	10,800	8,900-12,600	.252	.216-.284
24 Feb	9	1.00	.90-1.14	4.9	4.5-5.5	-2	-2 to -2	11,100	9,300-12,600	.309	.278-.328
26 Feb	11	0.97	.91-1.07	4.8	4.6-5.3	0	+1 to 0	10,600	9,500-11,200	.279	.256-.303
3 Mar	16	1.02	.94-1.16	5.3	4.9-5.9	+1	+2 to 0	9,000	7,600-9,800	.266	.236-.286
10 Mar	23	1.373	1.28-1.44	7.4	7.0-7.7	-3	-2 to -3	6,900	6,600-7,500	.355	.340-.368
12 Mar	25	0.90	.86-.92	5.0	4.6-5.2	+1	+2 to 0	10,600	10,000-11,100	.235	.230-.242
17 Mar	30	0.86	.76-.92	4.9	4.4-5.3	0	0 to 0	10,800	9,600-12,300	.219	.198-.234
19 Mar	32	0.93	.91-.96	5.0	4.9-5.1	-1	0 to -1	10,800	10,100-11,400	.252	.228-.270
24 Mar	37	0.85	.80-.92	4.9	4.5-5.1	+2	+2 to +2	10,900	9,900-11,500	.222	.207-.241
26 Mar	39	0.97	.82-1.07	5.5	4.4-5.6	-1	0 to -1	9,200	8,400-10,700	.236	.200-.265
31 Mar	44	0.80	.73-.88	5.0	4.8-5.4	--	--	10,900	9,700-11,800	.198	.175-.210
2 Apr	46	0.77	.69-.85	4.6	4.1-5.0	+1	+1 to -1	11,700	10,700-13,500	.193	.176-.218
7 Apr	51	0.84	.77-.90	4.8	4.6-5.0	0	+1 to 0	10,000	9,400-10,500	.200	.172-.220
9 Apr	53	0.78	.73-.82	4.7	4.5-4.9	+2	+3 to 0	10,700	10,100-11,100	.183	.171-.192
14 Apr	58	0.80	.75-.89	4.4	4.2-4.7	-2	-1 to -3	12,000	10,600-12,700	.208	.194-.232
16 Apr	60	0.92	.85-1.01	5.6	5.5-5.7	0	+1 to -2	9,000	8,500-9,500	.211	.193-.242
21 Apr	65	0.78	.74-.82	4.2	4.0-4.4	0	0 to 0	12,800	12,200-13,500	.216	.206-.225
23 Apr	67	0.80	.78-.86	4.7	4.4-5.2	-1	-1 to -2	11,200	10,200-12,100	.201	.190-.207
28 Apr	72	1.02	.96-1.04	5.5	5.3-5.8	-1	-1 to -1	8,700	8,400-8,900	.248	.225-.266
30 Apr	74	1.02	.94-1.07	6.0	5.5-6.4	0	0 to 0	8,200	8,000-8,500	.238	.209-.262
5 May	79	0.87	.86-.88	4.4	4.3-4.6	0	+1 to -1	10,600	10,200-11,000	.222	.210-.232
7 May	81	0.85	.81-.90	4.5	4.2-4.8	0	+1 to 0	10,500	9,600-11,800	.210	.195-.221
12 May	86	0.90	.84-1.01	4.9	4.7-5.3	+1	+2 to 0	9,600	9,400-9,700	.219	.191-.268
14 May	88	0.91	.83-.99	5.3	4.7-5.5	+1	+1 to 0	9,600	9,000-10,500	.216	.201-.243
19 May	93	0.94	.92-.96	5.5	5.4-5.6	-2	-2 to -2	10,000	9,800-10,300	.239	.232-.244

Table 8A. Hemodynamic Data from Pig-Tailed Monkey #58, Pindarus, during Continuous Restraint.
Aortic Blood Pressures and Heart Rate.

Date	Couch Day	Aortic Pressures				Heart Rate	
		Systolic Mean Range (mm Hg)	Diastolic Mean Range (mm Hg)	Pulse Mean Range (mm Hg)	Mean Range (mm Hg)	Mean Range (beats/min)	
16 Apr 65	8	137	93	43	113	180	
21 Apr	13	131	86	44	108	188-196	
23 Apr	15	131	85	46	107	168-196	
28 Apr	20	132	87	45	111	200-204	
30 Apr	22	142	95	47	118	180-184	
5 May	27	141	95	45	115	204-216	
7 May	29	125	82	43	101	192-200	
12 May	34	127	83	44	106	212-228	
14 May	36	120	83	37	101	168-176	
19 May	41	132	86	46	109	206-232	
21 May	43	143	96	47	117	176-200	
26 May	48	145	99	46	122	216-232	
28 May	50	124	86	38	105	172-176	
2 Jun	55	139	94	45	116	221	
4 Jun	57	124	84	40	104	172-180	
9 Jun	62	130	90	40	113	172-178	
11 Jun	64	145	101	44	120	196-204	
16 Jun	69	139	92	47	113	180-220	
18 Jun	71	154	105	49	125	176-200	
23 Jun	76	135	90	45	113	164-172	
25 Jun	78	122	83	39	102	156-156	
30 Jun	82	142	96	45	117	180-188	
2 Jul	84	124	84	40	106	156-164	
7 Jul	89	129	88	41	108	170-172	
9 Jul	91	140	97	46	115	156-172	

Table 8B. Hemodynamic Data from Pig-Tailed Monkey #58, Pindarus, during Continuous Restraint. Cardiac Output, Stroke Volume, Mean Venous Pressure, Systemic Resistance and Cardiac Work.

Date	Couch Day	Cardiac Output		Stroke Volume		Mean Venous Pressure		Systemic Resistance		Cardiac Work	
		Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range
		(liters/min)		(ml)		(mm Hg)		(dyne sec/cm ⁵)		(watts)	
16 Apr 65	8	0.45	.44-.45	2.5	2.5-2.5	-3	-2 to -4	20,800	20,300-21,300	.112	.108-.116
21 Apr	13	0.49	.47-.50	2.5	2.4-2.7	0	+1 to 0	17,900	16,700-19,200	.117	.111-.122
23 Apr	15	0.58	.56-.59	3.2	3.0-3.3	-3	-3 to -4	15,300	15,100-15,500	.136	.131-.145
28 Apr	20	0.87	.86-.89	4.3	4.3-4.4	-1	0 to -2	10,300	10,200-10,500	.213	.204-.224
30 Apr	22	0.70	.63-.75	3.9	3.4-4.1	-3	-2 to -4	13,800	12,500-15,700	.184	.166-.194
5 May	27	0.82	.80-.84	3.9	3.8-4.0	-3	-2 to -4	11,500	11,400-11,600	.208	.202-.214
7 May	29	0.80	.77-.85	4.1	4.0-4.3	-2	-1 to -4	10,200	9,700-10,700	.180	.171-.193
12 May	34	0.94	.92-.96	4.2	4.0-4.5	--	--	9,000	8,700-9,300	.220	.218-.224
14 May	36	0.72	.69-.74	4.2	4.1-4.4	--	--	11,300	11,000-11,900	.161	.155-.168
19 May	41	0.79	.72-.84	3.6	3.4-4.0	-1	0 to -2	11,000	10,500-11,600	.193	.162-.216
21 May	43	0.87	.81-.98	4.7	4.1-5.3	--	--	10,900	9,600-11,900	.219	.201-.233
26 May	48	0.96	.96-.97	4.4	4.2-4.5	-2	-1 to -3	10,300	9,900-10,800	.261	.251-.278
28 May	50	0.73	.71-.78	4.2	4.0-4.6	-3	-2 to -4	11,800	10,600-12,600	.170	.164-.174
2 Jun	55	0.87	.85-.89	4.0	3.8-4.1	-3	-3 to -4	11,100	10,900-11,400	.217	.210-.223
4 Jun	57	0.82	.67-1.01	4.7	3.8-5.6	-2	-2 to -3	10,600	8,700-12,700	.191	.157-.239
9 Jun	62	0.67	.61-.78	3.9	3.6-4.4	-3	-3 to -3	13,900	11,700-15,100	.169	.153-.190
11 Jun	64	0.74	.72-.76	3.7	3.7-3.8	-2	-1 to -2	13,100	12,900-13,300	.210	.189-.221
16 Jun	69	0.90	.80-1.05	4.7	4.5-4.8	-2	-1 to -2	10,300	9,100-11,200	.227	.196-.272
18 Jun	71	0.84	.77-.89	4.4	4.0-5.1	-3	-2 to -4	12,100	10,600-13,200	.236	.221-.242
23 Jun	76	0.79	.70-.91	4.7	4.2-5.3	-3	-1 to -4	11,800	9,900-13,100	.198	.174-.228
25 Jun	78	0.64	.60-.70	4.1	3.9-4.5	-2	-2 to -3	13,000	11,600-13,800	.145	.137-.155
30 Jun	82	0.87	.78-.93	4.8	4.2-5.2	-5	-5 to -5	11,200	10,300-13,000	.226	.212-.238
2 Jul	84	0.68	.64-.73	4.3	4.0-4.7	-4	-4 to -4	12,900	12,000-13,800	.161	.153-.170
7 Jul	89	0.78	.75-.80	4.5	4.4-4.7	-4	-3 to -4	11,500	11,100-11,900	.187	.181-.191
9 Jul	91	0.65	.60-.74	4.0	3.6-4.6	-4	-3 to -4	14,800	12,100-16,600	.167	.151-.177

Table 9A. Hemodynamic Data from Pig-Tailed Monkey #68, Alexas, during Continuous Restraint.
Aortic Blood Pressures and Heart Rate.

Date	Couch Day	Aortic Pressures				Heart Rate		
		Systolic		Diastolic		Mean	Range	
		Mean	Range	Mean	Range			
(mm Hg)	(mm Hg)	(mm Hg)	(mm Hg)	(mm Hg)	(beats/min)			
15 Feb 65	14	134	132-138	89	88-90	110	201	200-202
17 Feb	16	126	125-126	88	88-89	110	214	206-224
19 Feb	19	122	117-124	83	79-86	106	209	208-210
24 Feb	23	126	121-133	86	84-88	101	225	224-228
26 Feb	25	102	99-106	71	68-75	90	205	198-208
3 Mar	30	115	113-116	79	77-81	97	202	196-206
10 Mar	37	117	108-126	79	70-84	94	185	172-200
11 Mar	38	150	146-157	93	92-94	112	211	204-216
12 Mar	39	121	117-125	83	79-87	99	173	170-176
17 Mar	44	118	116-121	79	76-81	97	201	192-208
19 Mar	46	112	109-114	74	70-76	93	183	176-192
24 Mar	51	120	119-121	82	82-83	96	186	184-188
26 Mar	53	126	122-133	86	83-90	102	196	192-200
31 Mar	58	120	118-122	81	80-82	99	185	174-200
2 Apr	60	121	114-126	83	76-88	100	189	184-192
7 Apr	65	120	118-122	80	79-82	102	205	196-220
9 Apr	67	115	111-119	78	76-80	97	187	186-188
14 Apr	72	112	106-116	76	71-79	92	207	204-208
16 Apr	74	127	122-131	86	83-89	104	189	184-196
21 Apr	79	105	103-108	68	67-70	87	173	168-178
23 Apr	81	104	100-110	71	69-73	90	169	168-172
28 Apr	86	95	85-101	62	58-65	77	181	176-188
30 Apr	88	100	99-102	62	62-63	79	181	168-188
5 May	93	127	120-136	84	79-88	104	208	192-220

Table 9B. Hemodynamic Data from Pig-Tailed Monkey #68, Alexas, during Continuous Restraint. Cardiac Output, Stroke Volume, Mean Venous Pressure, Systemic Resistance and Cardiac Work.

Date	Couch Day	Cardiac Output		Stroke Volume		Mean Venous Pressure		Systemic Resistance		Cardiac Work	
		Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range
		(liters/min)	(ml)	(mm Hg)	(dyne sec/cm ⁵)	(watts)					
15 Feb 65	14	0.89	3.9-5.0	-3	-2 to -3	10,200	9,050-11,400	.222	.199-.246		
17 Feb	16	0.86	3.7-4.6	--	--	10,500	8,500-11,600	.210	.186-.254		
19 Feb	19	0.70	3.2-3.4	-1	0 to -2	12,300	11,900-12,700	.161	.155-.171		
24 Feb	23	0.87	3.6-4.4	+1	+2 to 0	9,100	8,200-9,900	.197	.178-.228		
26 Feb	25	0.82	3.5-4.7	+1	+2 to 0	8,800	7,400-9,800	.161	.148-.171		
3 Mar	30	0.67	3.0-3.8	--	--	11,600	11,000-12,200	.147	.134-.165		
10 Mar	37	0.87	4.4-5.1	+1	+1 to 0	8,700	8,200-9,500	.182	.168-.203		
11 Mar	38	0.97	4.1-5.3	-3	-3 to -4	9,500	8,500-10,800	.240	.216-.282		
12 Mar	39	0.65	3.6-3.9	0	0 to -1	12,100	12,000-12,200	.143	.137-.148		
17 Mar	44	0.67	3.2-3.5	0	0 to -1	11,600	11,100-12,000	.146	.138-.160		
19 Mar	46	0.66	3.3-4.0	-1	-1 to -1	11,500	10,000-12,400	.138	.119-.164		
24 Mar	51	0.54	2.9-2.9	0	+1 to 0	14,100	13,700-14,100	.115	.110-.123		
26 Mar	53	0.65	3.2-3.5	0	+1 to 0	13,000	12,000-13,400	.145	.142-.148		
31 Mar	58	0.61	2.9-4.0	-1	-3 to -1	13,300	12,000-14,300	.133	.120-.153		
2 Apr	60	0.55	2.7-3.1	+1	+3 to 0	14,400	13,800-15,500	.121	.115-.125		
7 Apr	65	0.66	3.0-3.7	+1	+2 to 0	12,300	11,100-13,200	.150	.137-.166		
9 Apr	67	0.53	2.5-3.3	--	--	14,800	13,000-16,200	.111	.099-.130		
14 Apr	72	0.62	2.8-3.2	0	+1 to -1	11,900	11,800-12,100	.127	.119-.135		
16 Apr	74	0.72	3.6-4.1	--	--	12,400	11,900-13,300	.168	.164-.172		
21 Apr	79	0.63	3.5-3.8	0	0 to -1	11,000	10,700-11,400	.123	.118-.126		
23 Apr	81	0.61	3.5-3.7	-2	-1 to -2	12,000	11,100-13,300	.123	.121-.125		
28 Apr	86	0.82	4.4-4.7	-2	-1 to -3	7,700	7,600-7,900	.139	.131-.145		
30 Apr	88	0.71	4.1-4.1	-1	0 to -1	9,000	8,600-9,200	.124	.116-.140		
5 May	93	0.65	2.9-3.4	+1	+3 to -1	12,900	12,100-13,100	.149	.142-.153		

Table 10. Effect of Blood Removal and Return on Heart Rate and Blood Pressure in Pig-Tailed Monkey #62, Bushy,
Body Weight 9.0 kg.

Date	Time of Day	Volume of Blood Withdrawn (ml)	Before Removal		During Removal		End of Removal		During Return		End of Return	
			Heart Rate (beats/min)	Aortic Pressure syst/diast (mm Hg)	Heart Rate (beats/min)	Aortic Pressure syst/diast (mm Hg)	Heart Rate (beats/min)	Aortic Pressure syst/diast (mm Hg)	Heart Rate (beats/min)	Aortic Pressure syst/diast (mm Hg)	Heart Rate (beats/min)	Aortic Pressure syst/diast (mm Hg)
31 Mar	1417	16.5	160	135/82	160	135/82	--	--	160	160	143/85	160
	1429	16.5	160	137/77	154	137/77	--	--	154	154	125/73	160
	1447	16.5	164	150/86	160	150/86	--	--	160	160	138/81	160
21 Apr	1431	17	188	157/91	184	157/91	188	148/91	192	192	166/95	192
	1447	14.5	184	156/90	184	156/90	--	--	184	184	161/86	186
	1505	13.5	188	161/97	182	161/97	180	154/91	184	184	157/90	180
23 Apr	1433	30	164	134/76	168	134/76	176	141/83	168	168	140/79	164
	1447	15	168	137/79	172	137/79	172	136/80	188	188	148/84	184
	1506	20	182	147/90	180	147/90	188	148/89	192	192	147/83	184
28 Apr	1525	30	184	136/84	192	136/84	190	142/86	192	192	150/85	192
	1450	17	188	125/79	192	125/79	--	--	192	192	144/79	188
	1505	30	190	136/78	192	136/78	192	133/77	192	192	132/74	192
30 Apr	1522	30	184	130/75	188	130/75	188	138/82	190	190	134/75	188
	1538	30	176	131/74	172	131/74	172	122/72	172	172	131/71	172
	1556	30	172	137/78	172	137/78	172	129/75	172	172	126/70	176
5 May	1553	30	192	142/81	192	142/81	200	150/91	196	196	132/81	196
	1610	30	192	141/95	192	141/95	196	151/87	196	196	142/83	194
	1624	30	202	154/88	198	154/88	198	146/89	196	196	163/89	208
7 May	1500	30	180	132/76	188	132/76	184	130/79	192	192	135/77	180
	1516	30	188	144/82	184	144/82	--	---	--	--	--	--
	1535	30	192	150/89	188	150/89	188	137/84	188	188	155/85	192
14 May	1502	30	172	147/83	172	147/83	172	137/81	188	188	147/81	176
19 May	1415	30	170	147/87	170	147/87	172	147/88	172	172	152/86	172

Table 11. Twenty-four Hour Hemodynamic Trial on Pig-Tailed Monkey #56, Titinius.

Date & Time	Heart Rate (beats/min)	Cardiac Output (liters/min)	Stroke Volume (ml)
3 Feb 65			
1000	186	0.79	4.2
1100	192	0.91	4.7
1200	196	0.92	4.7
1300	198	0.86	4.4
1400	200	1.02	5.1
1500	204	0.88	4.3
1600	204	0.95	4.7
1700	204	1.12	5.5
1800	194	1.02	5.3
1900	196	0.98	5.0
2000	204	1.28	6.3
2100	196	1.01	5.2
2200	200	1.14	5.7
2300	196	0.90	4.6
2400	188	1.06	5.6
4 Feb 65			
0100	186	1.04	5.6
0200	174	1.00	5.8
0300	186	0.96	5.2
0400	176	0.92	5.5
0500	166	0.91	5.5
0600	168	0.95	5.6
0700	156	0.89	5.3
0800	172	0.94	5.5
0900	180	0.84	4.7
1000	184	0.86	4.7

Table 12. Twenty-four Hour Hemodynamic Trial on Pig-Tailed Monkey #68, Alexas.

Date and Time	Heart Rate (beats/min)	Aortic Pressures				Venous Pressure (mm Hg)
		Systolic (mm Hg)	Diastolic (mm Hg)	Pulse (mm Hg)	Mean (mm Hg)	
3 Feb 65						
1000	232	136	101	35	118	-1
1100	236	138	97	41	118	-1
1200	240	132	95	37	110	0
1300	232	134	91	43	--	--
1400	222	119	75	44	100	0
1500	228	115	74	41	96	0
1600	236	123	83	40	100	0
1700	234	117	79	38	98	-2
1800	228	111	75	36	95	-3
1900	218	120	80	40	95	-2
2000	204	124	83	41	98	0
2100	212	116	76	40	95	0
2200	206	117	79	38	96	-1
2300	212	127	89	38	103	+1
2400	218	120	82	38	100	0
4 Feb 65						
0100	208	115	82	33	96	-1
0200	204	120	85	35	100	0
0300	196	110	74	36	90	0
0400	200	108	73	35	90	+1
0500	204	108	74	34	90	+1
0600	208	105	71	34	92	0
0700	208	102	84	36	100	0
0800	212	109	80	29	90	0
0900	220	116	81	35	98	0
1000	220	120	84	36	105	+1

Table 13. Hemodynamic Effects of Isoproterenol on Pig-Tailed Monkey #68, Alexas.

Time of Day	Aortic Pressures			Heart Rate (beats/min)	Cardiac Output (liters/min)	Stroke Volume (ml)	Systemic Resistance (dyne sec/cm ⁵)	Cardiac Work (watts)	
	Systolic (mm Hg)	Diastolic (mm Hg)	Pulse (mm Hg)						Mean (mm Hg)
<u>Pre-injection control</u>									
1202	122	79	43	100	176	.767	4.4	10,400	.170
<u>.02 mg Isoproterenol injected</u>									
1208									
1210	130	80	50	103	240	.958	4.0	8,600	.219
1223	126	85	41	106	188	.748	4.0	11,400	.176
1338	132	87	45	110	194	.765	3.9	11,500	.187
<u>.032 mg Isoproterenol injected</u>									
1341									
1342	118	53	65	86	272	1.028	3.8	6,700	.196
<u>2 ml of 0.9% saline injected</u>									
1409									
1410	116	78	38	95	188	.620	3.3	12,500	.131

Table 14. Hemodynamic Effects of Hypothermia on Pig-Tailed Monkey #55, Verges.

Time of Day	Esophageal Temp. (°C)	Rectal Temp. (°C)	Respiratory Rate (breaths/min)	Aortic Pressures				Heart Rate (beats/min)	Cardiac Output (liters/min)	Stroke Volume (ml)	Systemic Resistance (dyne sec/cm ⁵)	Cardiac Work (watts)
				Systolic (mm Hg)	Diastolic (mm Hg)	Pulse (mm Hg)	Mean (mm Hg)					
1126	34.9	35.2	20	157	112	45	136	172	0.67	3.9	16,200	.202
1142	33.7	34.0	17	141	97	44	121	156	0.57	3.7	17,000	.153
1153	31.6	31.9	16	152	106	46	127	132	0.54	4.1	18,800	.139
1208	29.9	29.9	14	155	107	48	132	120	0.46	3.8	23,000	.135
1222	28.2	28.4	14	152	107	45	130	92	0.33	3.6	31,600	.095
1233	26.8	27.0	16	155	106	49	127	80	0.30	3.8	34,000	.085
1247	25.3	25.6	12	142	100	42	125	76	0.27	3.6	37,100	.075

Table 15. Total Body Water Measurements and Total Body Fat Estimates in 8 Pig-Tailed Monkeys.

No.	Name	Total Body Weight (kg)	Total Body Water		Total Body Fat		Fat-Free Body Weight		T ₂ O Body Clearance Half-Time (days)
			(liters)	(%)	(kg)	(%)	(kg)	(%)	
20	Benvolio	8.69	5.80	66.8	0.76	8.7	7.93	91.3	6.4
32	Touchstone	7.76	5.21	67.1	0.64	8.3	7.12	91.7	6.9
49	Claudius	7.21	4.64	64.4	0.87	12.0	6.34	88.0	6.4
56	Titinius	7.34	4.86	66.2	0.70	9.6	6.64	90.4	4.5
35	Nestor	7.29	5.14	70.6	0.26	3.6	7.03	96.4	4.3
62	Bushy	9.87	6.69	67.8	0.73	7.4	9.14	92.6	9.5
68	Alexas	6.80	4.32	63.4	0.91	13.4	5.89	86.6	5.7
58	Pindarus	7.04	4.53	64.4	0.85	12.0	6.19	88.0	5.3
	Mean	7.75	5.15	66.3	0.72	9.4	7.03	90.6	6.1